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- (63) Related by continuation (CON) or continuation-in-part (CIP) to earlier application: US 60/194,336 (CIP) Filed on 3 April 2000 (03.04.2000) (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
- (71) Applicant (*for all designated States except US*): THE GOVERNMENT OF THE UNITED STATES OF AMERICA, as represented by THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES [US/US]; c/o National Institutes of Health, Office of Technology Transfer, 6011 Executive Boulevard, Suite 325, Rockville, MD 20852-3804 (US).
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- (75) Inventors/Applicants (*for US only*): MORIN, Patrice, J. [CA/US]; 8131 Greenspring Valley Road, Owings Mills, MD 21117 (US). SHERMAN-BAUST, Cheryl, A. [US/US]; 8811 Baker Avenue, Baltimore, MD 21234 (US). PIZER, Ellen, S. [US/US]; 5962 Camelback
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: TUMOR MARKERS IN OVARIAN CANCER

(57) Abstract: The present invention features methods of diagnosing and prognosticating ovarian tumors by detecting increased expression of an ovarian tumor marker gene in a subject or in a sample from a subject. Also featured are kits for the aforementioned diagnostic and prognostic methods. In addition, the invention features methods of treating and preventing ovarian tumors, and methods of inhibiting the growth or metastasis of ovarian tumors, by modulating the production or activity of an ovarian tumor marker polypeptide. Further featured are methods of inhibiting the growth or metastasis of an ovarian tumor by contacting an ovarian tumor cell with an antibody that specifically binds an ovarian tumor marker polypeptide.

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WO 01/075177 A3

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/10947

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, CHEM ABS Data, EMBASE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 53040 A (SCHMITT ARMIN ;SPECHT THOMAS (DE); DAHL EDGAR (DE); HINZMANN BERND) 21 October 1999 (1999-10-21) Tabelle I, SEQ ID NO:72 --- -/-	1-22,28, 29,32

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

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"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"Z" document member of the same patent family

Date of the actual completion of the international search

1 October 2002

Date of mailing of the international search report

10. 01. 2003

Name and mailing address of the ISA

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## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 01/10947

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>HOUGH COLLEEN D ET AL: "Comparison of sage-generated expression profiles between ovarian cancer and human ovarian surface epithelium." PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL, no. 41, March 2000 (2000-03), pages 310-311, XP008008525 91st Annual Meeting of the American Association for Cancer Research.;San Francisco, California, USA; April 01-05, 2000, March, 2000 ISSN: 0197-016X the whole document</p> <p>---</p>	
A	<p>HOUGH C D ET AL: "Use of SAGE to study gene expression in ovarian cancer." PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL, vol. 40, March 1999 (1999-03), page 34 XP008008524 90th Annual Meeting of the American Association for Cancer Research;Philadelphia, Pennsylvania, USA; April 10-14, 1999, March, 1999 ISSN: 0197-016X the whole document</p> <p>---</p>	
A	<p>DEPASQUALE S E ET AL: "Differential expression of the pRb2 tumor suppressor gene in human epithelial ovarian carcinoma compared to ovarian tumors of low malignant potential and normal ovaries." PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL, vol. 38, 1997, page 109 XP008008526 Eighty-eighth Annual Meeting of the American Association for Cancer Research;San Diego, California, USA; April 12-16, 1997, 1997 ISSN: 0197-016X the whole document</p> <p>---</p>	
A	<p>MOK SAMUEL C ET AL: "Molecular Cloning of Differentially Expressed Genes in Human Epithelial Ovarian Cancer." GYNECOLOGIC ONCOLOGY, vol. 52, no. 2, 1994, pages 247-252, XP002128355 ISSN: 0090-8258 page 247, right-hand column, paragraph 1 page 248, right-hand column, last paragraph page 251, right-hand column</p> <p>---</p>	

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## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 01/10947

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,A	<p>HOUGH COLLEEN D ET AL: "Large-scale serial analysis of gene expression reveals genes differentially expressed in ovarian cancer." CANCER RESEARCH, vol. 60, no. 22, 15 November 2000 (2000-11-15), pages 6281-6287, XP002215320 ISSN: 0008-5472 the whole document -----</p>	

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 01/10947

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☒ Claims Nos.: 30  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Claims (1-22, 28, 29 and 32) - partially; claim 30 - completely

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

International Application No. PCT/US 01/10947

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## Continuation of Box I.1

Claim 6 and, as far as an "in vivo" method is concerned, claims 1-3, 7-13 and 19-21 and partially 22, 28 and 29 are directed to a diagnostic method practised on the human/animal body and the search has been carried out and based on the alleged effects of the compound/composition.

Claims 14-18 and partially claims 22, 28 and 29 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

## Continuation of Box I.2

Claims Nos.: 30

Claim 30 refers to an antibody without giving a true technical characterization. Moreover, no such compounds are defined in the application. In consequence, the scope of said claim is ambiguous and vague, and its subject-matter is not sufficiently disclosed and supported (Art. 5 and 6 PCT). No search can be carried out for purely speculative claims whose wording is, in fact, a mere recitation of the results to be achieved.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

International Application No. PCT/US 01/10947

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: Claims (1-22, 28, 29 and 32) - partially; claim 30 - completely

Methods for detecting/diagnosing ovarian cancer or the predisposal to develop it, as well as a method to determine the effectiveness of a treatment against ovarian cancer, all comprising measuring the expression of the alpha prothymosin gene (SEQ ID NO:1). Method of treating or preventing ovarian cancer comprising modulating production or activity of the polypeptide encoded thereby (SEQ ID NO:2). Kit comprising the polynucleotide of the invention.

Inventions 2-19: Claims (1-22, 25, 28, 29, 31, 32 and 35) - partially

Invention 2: Methods for detecting/diagnosing ovarian cancer or the predisposal to develop it, as well as a method to determine the effectiveness of a treatment against ovarian cancer, all comprising measuring the expression of the beta polypeptide 2-like G protein subunit 1 gene (SEQ ID NO:3) or its tag SEQ ID NO:84. Method of treating or preventing ovarian cancer comprising modulating production or activity of the polypeptide encoded thereby (SEQ ID NO:4). Kits comprising the polynucleotides of the invention.

Ibidem for inventions 3-19, but restricted to each one of the other markers mentioned in claims 22 and 32: Invention 3 refers to Lutheran blood group (B-CAM) (SEQ ID NOs:5, 6 and 85) ... invention 19 refers to eIF-2-associated p67 (SEQ ID NOs:38, 39 and 102).

Inventions 20-40: Claims (1-21, 23, 26, 28, 29, 31, 33 and 36) - partially

Invention 20: Methods for detecting/diagnosing ovarian cancer or the predisposal to develop it, as well as a method to determine the effectiveness of a treatment against ovarian cancer, all comprising measuring the expression of the HLA-DR alpha chain gene (SEQ ID NO:40) or its tag SEQ ID NO:103. Method of treating or preventing ovarian cancer comprising modulating production or activity of the polypeptide encoded thereby (SEQ ID NO:41). Kits comprising the polynucleotides of the invention.

Ibidem for inventions 21-40, but restricted to each one of the other markers mentioned in claims 23 and 33: Invention 21 refers to cysteine-rich protein 1 (SEQ ID NOs:42, 43 and 104) ... invention 40 refers to HLA-Cw (SEQ ID NOs:81, 82 and 129).

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Inventions 41-43: Claims (1-21, 24, 27-29, 31, 34 and 37) - partially

Invention 41: Methods for detecting/diagnosing ovarian cancer or the predisposal to develop it, as well as a method to determine the effectiveness of a treatment against ovarian cancer, all comprising measuring the expression of the HOST-3 (Claudin-16) gene (SEQ ID NO:141). Method of treating or preventing ovarian cancer comprising modulating production or activity of the polypeptide encoded thereby (SEQ ID NO:142). Kit comprising the polynucleotide of the invention.

Ibidem for inventions 42 and 43, but restricted to each one of the other markers mentioned in claims 24 and 34:

Invention 42 refers to HOST-4 (SEQ ID NO:144) and invention 43 refers to HOST-5 (SEQ ID NOs:146 and 147).

Inventions 44-49: Claims (1-21, 26, 28, 29, 31 and 36) - partially

Invention 44: Methods for detecting/diagnosing ovarian cancer or the predisposal to develop it, as well as a method to determine the effectiveness of a treatment against ovarian cancer, all comprising measuring the expression of the gene tag SEQ ID NO:106. Method of treating or preventing ovarian cancer comprising modulating production or activity of the polypeptide encoded thereby. Kit comprising the polynucleotide of the invention.

Ibidem for inventions 45-49, but restricted to each one of the other tags mentioned in claims 26 and 36: Invention 45 refers to tag SEQ ID NO:107 ... invention 36 refers to tag SEQ ID NO:122.

Inventions 50-51: Claims (1-21, 27-29, 31 and 37) - partially

Invention 50: Methods for detecting/diagnosing ovarian cancer or the predisposal to develop it, as well as a method to determine the effectiveness of a treatment against ovarian cancer, all comprising measuring the expression of the gene tag SEQ ID NO:143. Method of treating or preventing ovarian cancer comprising modulating production or activity of the polypeptide encoded thereby. Kit comprising the polynucleotide of the invention.

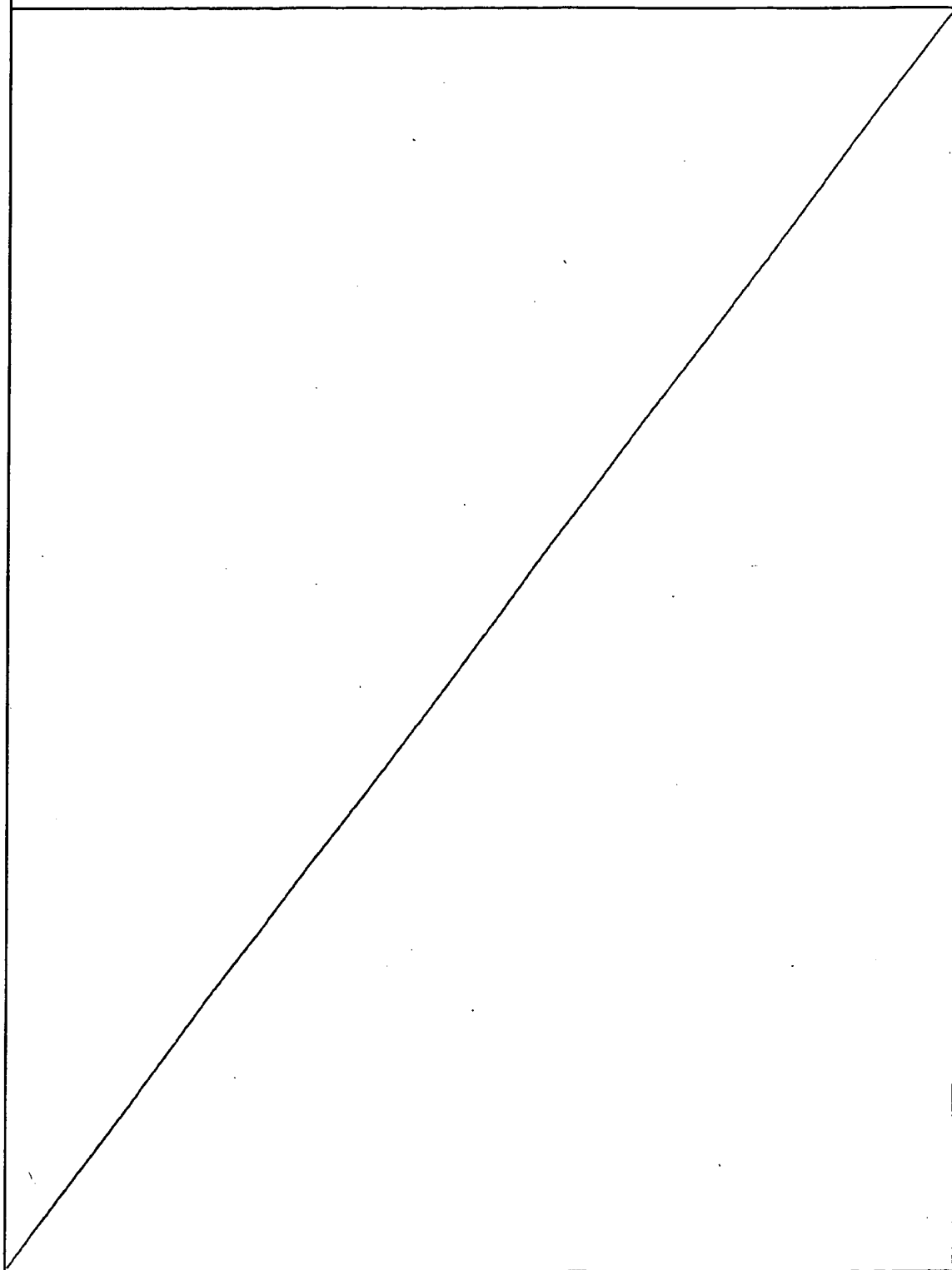
Ibidem for invention 51, but restricted to the other tag mentioned in claims 27 and 37 (tag SEQ ID NO:145).



INTERNATIONAL SEARCH REPORT

International Application No. PCT/US 01/10947

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210



# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/10947

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9953040	A	21-10-1999	DE 19817557 A1	21-10-1999
			WO 9953040 A2	21-10-1999
			EP 1073727 A2	07-02-2001
			JP 2002511252 T	16-04-2002
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